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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,063	01/22/2002	Muharrem Gokcen	8004.4USC1	6838

23552 7590 03/26/2004

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,063	GOKCEN, MUHARREM	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-58* is/are pending in the application.

4a) Of the above claim(s) *53 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-52 and 54-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/1/02*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *032404* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Gokcen, M.

Date of priority: 10/28/99

Claims 33-58 are pending in the application.

Claim 53 and 58 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 33-52, and 54-57 are currently under prosecution.

DETAILED ACTION

The Election filed 1/26/04 in response to the Office Action mailed 11/17/2003 is acknowledged and has been entered.

Applicant's election with traverse of Group I, claims 33-57 is acknowledged. The traversal is on the ground(s) that sufficient reasons and/or examples to justify a Restriction Requirement have not been provided. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the action mailed 11/17/2003. Furthermore, the groups are classified differently necessitating different searches in the literature and different considerations with regards to patentability. Applicants further traverse a species election requirement as searching the species would present no undue burden on the Examiner. This argument has been considered but is not found relevant because an election of species was not required in the action mailed 11/17/03. Instead, Group I was further restricted into

independent and or distinct groups based on improper Markush grouping of distinct enzymes (see page 3 of Action mailed 11/17/03). Upon election of Group I, Applicant was further required to elect one enzyme for examination on the merits as each enzyme constituted a distinct group. In order to promote compact prosecution, a call was placed to Mark T. Skoog to clarify that the additional election of an enzyme was not a species election (See attached Interview Summary). Applicant's agreed that the restriction requirement did not include an election of species and elected to prosecute the claims drawn to the **glycosidase** enzyme (Group A, page 3, Action mailed 11/17/03) .

For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claim Objections

Claim 39 is objected to because it includes independent and or distinct compositions drawn to non-elected inventions. This objection can be obviated by amending the claims to a composition further comprising a glycosidase.

Claims 33 is also objected to for reciting "colleganse" which appears to be misspelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41 and 54 contains the trademark/trade name TritonX®-100. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a nonionic surfactant and, accordingly, the identification/description is indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-52, and 54-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating localized prostate cancer comprising local administration of a composition comprising a therapeutically effective concentration of collagenase, hyaluronidase, calcium ions, a nonionic surfactant, an antibiotic, and a pharmaceutically acceptable aqueous carrier having a physiologic pH does not reasonably provide enablement for the claims as broadly drawn. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method of alleviating or curing prostate cancer comprising administering a composition comprising various therapeutically effective concentrations of enzymes such as: collagenase and calcium ions (Claim 33) **or** collagenase, calcium ions, and hyaluronidase (Claim 33,37), **or** collagenase, calcium ions, and a glycosidase (Claim 33, 39), **or** collagenase, calcium ions, and a nonionic surfactant (Claim 33, 40), **or** collagenase, calcium ions, and an antibiotic. The claims are further drawn to curing a prostate tumor in a mammal comprising effective concentrations of calcium ions, collagenase, hyaluronidase, a nonionic surfactant, and an antibiotic (Claim 50). hyaluronidase comprising a multitude of various enzymes and calcium ions.

The specification teaches (page 3) that the terms "treatment" and "treating" include the prevention and curing of prostate cancer or alleviating the metastasis of prostate cancer. The specification further teaches that curing prostate cancer includes degrading a prostate tumor such that a tumor cannot be detected after treatment. With regards to the treatment of advanced and or metastatic prostate cancer, the specification teaches (page 3) that alleviating metastasis of prostate cancer "includes" reducing the rate at which the prostate cancer spreads to other organs. Preventing metastasis of prostate cancer "includes" preventing the prostate cancer from

spreading outside of the prostate. Thus, based on the teachings of the specification, the claimed method includes curing or preventing "metastatic" prostate cancer.

However, one cannot extrapolate the teachings of the specification to the scope of the claims because, as written, the claims include curing or preventing prostate cancer and it is well established in the field of oncology that the prevention and or cure of cancer (including prostate cancer) can be highly unpredictable. First, it is noted that the claimed method involves the physical, enzymatic degradation of prostate tissue by administering therapeutic compositions of enzymes directly to the tissue. Thus, it is not practical or conceivable that the claimed method would predictably *prevent* prostate cancer in patients who have not been diagnosed with the disease. Secondly, it would not be predictable, nor is there evidence thereof, that the claimed method would effectively alleviate or cure metastatic prostate cancer. Prostate cancer is the most common male cancer in the United States, accounting for 32% of all newly diagnosed cancers, and is the second leading cause of death by cancer, accounting for 13% of cancer deaths in men. Conventional treatments include radical prostatectomy, radiotherapy, and hormonal therapy wherein said treatments may be reasonably predictive of long-term survival in patients whose cancer is *confined* to the prostate gland. However, in those patients where the cancer has spread beyond the prostate gland, a complete cure is rather unpredictable where metastasis to bone may be the predominant event leading to death (Murphy *et al.*, Clinical Oncology, 2nd edition, American Cancer Society, 1995, pages 315-318). Furthermore, as written, the claims require "local" administration or "direct" injection of the composition for therapeutic efficacy and it would not be predictable that such a composition would effectively target to distant metastatic cites and or effectively kill prostate cancer cells which have spread to other organ systems. Thus,

since the claimed method is not conventional in the art, and since the specification fails to teach the prevention or alleviation of metastatic prostate cancer, it would require undue experimentation to practice the invention as claimed. Thus, only a method of treating "localized" prostate cancer is enabled.

Further, with regards to the therapeutic composition, the specification teaches (examples 1 and 2, pages 23 and 24) that an effective concentration of hyaluronidase is added in addition to collagenase for the treatment of localized prostate cancer. The specification, however, is silent on the guidance and predictability of administering collagenase and calcium ions alone, collagenase, calcium ions, and a nonionic surfactant alone, collagenase, calcium ions, and an antibiotic alone, or collagenase, calcium ions and a genus of glycosidases alone. Moreover, the specification teaches (page 20) a whole host of disadvantages involving enzymatic ablation of tumor tissue including the short circulating half-lives of exogenously administered enzymes, development of immunological responses to foreign proteins, inhibition from antiproteinase effectors, or the inability to specifically target the enzymes to nodular areas of pathology. Thus, in the absence of objective evidence and in addition to the disadvantages taught, it would not be predictable that any other compositions would effectively substitute for the successful combination of hyaluronidase and collagenase. Further, the art only recognizes the combination of hyaluronidase and collagenase wherein Darson et al. proposes that the action of collagenase works by degrading collagen into small peptides by hydrolysis at several sites along its triple helix, and hyaluronidase works by digesting hyaluronic acid and thereby increasing the permeability of the connective tissue ground substance through direct enzymatic liquefaction (Darson et al. Mayo Clin.Proc., Vol. 73, 1998, page 908, IDS). Reasonable correlation must

exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted that collagenase alone or collagenase with any other enzymes other than hyaluronidase would effectively treat localized prostate cancer in the absence of objective evidence. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art such as the treatment of cancer. In the instant case, the claims are so broadly drawn, the guidance is so limited, and the art is so unpredictable that the skilled artisan is presented with a multitude of alternatives with no guidance as to which will enable use of the invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33, 35-37, 39-52, 54-57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6428785. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope and content of the patented claims includes nearly all of the

limitations of the pending claims. For example, patented Claim 1 falls within the scope of pending Claims 33, 35-37, 39-40, 42-44, and 50.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

March 25, 2004

GARY NICKOL
PRIMARY EXAMINER